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Bacillus intermedius ribonuclease as inhibitor of cell proliferation and membrane current

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Abstract

The antiproliferative action of the guanine-specific ribonuclease secreted by *Bacillus intermedius* (binase) was studied in different chicken and mouse cell lines. The proliferation rate of chicken embryo fibroblasts, either normal or Rous sarcoma virus-transformed, was significantly reduced by binase treatment. Among mouse fibroblasts, v-*ras*-transformed NIH3T3 cells were sensitive to binase, whereas the growth of non-transformed, v-*src*-transformed or v-*fms*-transformed NIH3T3 cells was not affected. A 48 h treatment with binase inhibited the Ca^{2+}-dependent K^+ current of v-*ras*-transformed NIH3T3 cells but had no effect on this membrane current in non-transformed and in v-*src*- or v-*fms*-transformed NIH3T3 cells. Our results suggest that mammalian cells expressing the *ras*-oncogene are a potential target for the antiproliferative action of binase.

Keywords: *Bacillus intermedius* RNase (binase); Chicken embryo fibroblasts; Mouse fibroblasts; Transformation; Proliferation; Ca^{2+}-dependent K^+ current

1. Introduction

A number of ribonucleases, such as binase (*Bacillus intermedius* RNase), pancreatic RNase A, bovine seminal ribonuclease, and RNase from oocytes of *Rana pipiens* (onconase) were shown to possess enzymatic and biological activities which may be exploited for the development of novel cytotoxic agents (Youle et al., 1993; Di Donato et al., 1994; Mikulski et al., 1995; Boque and Wlodawer, 1996; Prior et al., 1996). To assess the possibilty of a future clinical application of bacterial ribonucleases, the toxicity of these enzymes in various cell lines is currently under investigation. Compared to pancreatic RNase A, binase is a more effective growth inhibitor of Ehrlich ascites tumor cells and also of the ascitic form of lymp-

Abbreviations: CEF, chicken embryo fibroblast; EGTA, ethyleneglycol-bis(β-aminoethyl)-*N*,*N*,*N*',*N*'-tetraacetic acid; HEPES, 2-[4-(2-hydroxyethyl)-1-piperazine]-ethanesulfonic acid; LPA, lysophosphatidic acid; RNA, ribonucleic acid; RNase, ribonuclease; RSV, Rous sarcoma virus.

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